REMARKS

STATUS OF THE CLAIMS

Claims 1-26 are pending. Claims 9, 15, and 21 have been amended herein to merely correct a typographical error. No new matter has been added.

THE III2R AND H2F ANTIBODIES

In a teleconference with the undersigned the Examiner has indicated the entire amino acid sequences of the antibodies must be provided or that hybridomas expressing the antibodies need to be deposited.

Applicants argue that only the amino acid sequence from the framework region of the III2R and H2F antibodies is required to be disclosed to one of ordinary skill in the art to make and use the invention. These sequences are available in Manheimer-Lory, J. Exp. Med., 174:1639-1652 (1991).

Applicants believe that there has been a misunderstanding regarding the invention. In this invention, a chimeric antibody was made by combining the constant region of a human immunoglobulin (such as IgG2 or IgG4) with a variable region of a non-human antibody (such as the mouse 3D1 antibody). This chimeric antibody was then humanized. This process entailed comparing the sequence of the variable regions of the chimeric antibody to the published sequence of the variable regions of two human antibodies (III2R and H2F).[1] During this comparison of the printed sequences of the

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[1] The published sequences of the III2R and H2F antibodies were obtained from Manheimer-Lory, A. *et al., J. Exp. Med.* 174(6):1639-52 (1991).

variable regions of the antibodies, the inventors examined the framework sequences of the chimeric antibody and then modified them on the cDNA level to more closely resemble the natural sequences in the framework region of a human antibody based on the sequences of the III2R and/or H2F antibodies (i.e. certain non-human framework amino acids were substituted with corresponding human framework amino acids).

The Examiner appears to believe that the III2R and H2F antibodies were used as reagents in the preparation of the claimed invention. This is not the case.

Namely, portions of the III2R and H2F antibodies were not physically spliced and inserted into the chimeric antibody. Rather, Applicants relied on the printed and disclosed sequences of the variable regions in Manheimer-Lory and compared them on paper to the variable region sequences of the chimeric antibody to determine appropriate alterations to be made to the non-human portion of the chimeric antibody. Thus, the III2R and H2F antibodies themselves were never physically used as reagents to arrive at the claimed invention. Because the antibodies themselves were not used as reagents, Applicants argue that it is not necessary for the entire amino acid sequences of these antibodies or hybridomas that produce these antibodies to be disclosed.

This concept is illustrated at page 36, lines 14-17, which states that "based on a sequence homology, I2R [III2R] was selected to provide the framework for the humanized 3D1 heavy chain and H2F was selected for the humanized 3D1 light chain variable region." (Citing Manheimer-Lory). The specification at page 39, lines 13-14 says that "the CDRs in the humanized 3D1 heavy and light chains can accommodate substitutions of amino acids from the corresponding positions of I2R [III2R] frameworks."

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The 3D1 Antibody

Applicants hereby submit the entire nucleotide and amino acid sequence for the 3D1 antibody in paper form, thereby making the antibody available to the public. A sequence listing containing the nucleotide and amino acids is submitted separately. Accordingly, Applicants have obviated the concerns expressed by the Examiner in the teleconference with the undersigned.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration and re-examination of this Application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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Dated: October 15, 2002

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APPENDIX

9. (Amended) The method of claim 7, wherein said immunoglobulin further comprises a constant region comprising a human IgG2[M3] isotype.

15. (Amended) The method of claim 13, wherein said immunoglobulin further comprises a constant region comprising a human IgG2[M3] isotype.

21. (Amended) The method of claim 19, wherein said immunoglobulin further comprises a constant region comprises a human IgG2[M3] isotype.

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